

In the Claims

Claims 1-26 (Cancelled)

Claim 27 (New): A composition of matter comprising:

- a) an isolated or purified modified erythropoietin construct (MEC) selected from the group consisting of: SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, and truncated modified erythropoietin constructs of lengths X to Y, wherein X is an integer selected from 1, 2, 3, 4, 5, or 6 and Y is an integer selected from 188, 189, 190, 191, 192, or 193; or
- b) an isolated or purified modified erythropoietin construct according to a), further comprising a heterologous polypeptide sequence; or
- c) an isolated MEC of a) or b), and a carrier or diluent; or
- d) an isolated, purified, or recombinant nucleic acid encoding a MEC according to a) or b); or
- e) an isolated, purified, or recombinant nucleic acid according to d), further comprising regulatory elements, vector elements, or other nucleic acid elements; or
- f) a host cell transformed with an isolated nucleic acid according to d) or e); or
- g) an isolated, purified or recombinant polynucleotide sequence comprising a sequence encoding a polypeptide sequence selected from the group consisting of SEQ ID NO: 10, 11, 12, 13, 14, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, and 244; or

- h) an isolated, purified or recombinant polynucleotide sequence comprising a complementary polynucleotide sequence to a polynucleotide sequence encoding a polypeptide sequence selected from the group consisting of SEQ ID NO: 10, 11, 12, 13, 14, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, and 244; or
- i) an isolated, purified or recombinant polynucleotide sequence comprising a polynucleotide sequence having at least about 20% to 99.99% identity to a polynucleotide sequence of g) or h); or
- j) a fragment of a polynucleotide sequence according to g) or h); or
- k) a peptide, polypeptide, protein, or antibody having reduced immunogenicity as compared to the naturally occurring form of the peptide, polypeptide, or protein while retaining at least 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100% of the biological activity of the unmodified or naturally occurring molecule and said reduced immunogenicity is the result of reduced binding to MHC Class II molecules; or
- l) a peptide, polypeptide, or protein according to k), wherein the peptide, polypeptide, or protein is a therapeutic peptide, polypeptide, protein or antibody used in the diagnosis or treatment of diseases, conditions, or disorders; or
- m) a peptide, polypeptide, protein, or antibody according to c) or k), wherein the peptide, polypeptide, or protein comprises all, or a portion of, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-15, IL-16, IL-18, IL-19, IL-23, IL-24, erythropoietin (EPO), insulin, human growth hormone, calcitonin, Factor VIII, G-

CSF, M-CSF, GM-CSF platelet derived growth factor (PDGF), MSF, FLT-3 ligand, EGF, fibroblast growth factor (FGF); human insulin alpha, human insulin beta, insulin-like growth factors; vascular endothelial growth factor (VEGF; interferons; leukemia inhibitory factor (LIF); ciliary neurotrophic factor (CNTF); oncostatin M; stem cell factor (SCF); transforming growth factors; chemokines, or antibodies selected from the group consisting of REMICADE® (Infliximab); REOPRO® (Abciximab); SIMULECT® (Basiliximab); ZENAPAX® (Daclizumab); HERCEPTIN® (Trastuzumab); SYNAGIS® (Palivizumab); and XOLAIR® (Omalizumab); or

- n) a peptide, polypeptide, protein, or antibody according to m), wherein the protein is EPO and comprises a sequence selected from the group consisting of SEQ ID NOs: 10, 11, 12, 13, 14, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, and 244; or
- o) an isolated, purified, or recombinant erythropoietin (EPO) polypeptide containing a substituted peptide segment, wherein said substituted peptide segment is located at positions G101-Q115 (SEQ ID NO: 40) or D136-R150 (SEQ ID NO: 47), and said substituted peptide segment contains at least one amino acid substitution; or
- p) an isolated protein of n), comprising an amino acid sequence selected from the group consisting of: SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; SEQ ID NO:13; SEQ ID NO:14; SEQ ID NO:152; SEQ ID NO:154; SEQ ID NO:155; SEQ ID NO:159; SEQ ID NO:162; SEQ ID NO:181; SEQ ID NO:187; SEQ ID NO:199; SEQ ID NO:225; SEQ ID NO:226; SEQ ID NO:227; SEQ ID NO:228; SEQ ID NO:229; and SEQ ID NO:233; SEQ ID NO:245; SEQ ID NO:246; and SEQ ID NO:247; or
- q) a peptide, polypeptide, protein, or antibody according to k), l), m), n), o), or p), and a carrier or pharmaceutically acceptable excipient; or
- r) an isolated, purified, or recombinant polynucleotide encoding a peptide, polypeptide,

- protein and/or antibody according to k), l), m), n), o), or p); or
- s) an isolated, purified, or recombinant polynucleotide according to r), further comprising regulatory elements selected from promoters, enhancers, termination sequences, and combinations thereof; or
  - t) a vector comprising an isolated, purified, or recombinant polynucleotide according to r) or s); or
  - u) a host cell comprising an isolated, purified, or recombinant polynucleotide according to r), s), or t); or
  - v) an isolated, purified, or recombinant EPO polypeptide according to o), wherein said EPO polypeptide contains substituted peptide segments at positions G101-Q115 (SEQ ID NO: 40) and D136-R150 (SEQ ID NO: 47); or
  - w) an isolated, purified, or recombinant EPO polypeptide of o) or v), wherein said peptide segments are selected from those peptides set forth in Tables 10A, 10B, 11A, 11B, 12, 13A, 13B, 14A, 14B, or 14C; or
  - x) an isolated, purified, or recombinant EPO polypeptide of claims o) or v), wherein said peptide segment is selected from the group consisting of: SEQ ID NO:152; SEQ ID NO:154; SEQ ID NO:155; SEQ ID NO:159; SEQ ID NO:162; SEQ ID NO:181; SEQ ID NO:187; SEQ ID NO:199; SEQ ID NO:225; SEQ ID NO:226; SEQ ID NO:227; SEQ ID NO:228; SEQ ID NO:229; and SEQ ID NO:233; SEQ ID NO:245; SEQ ID NO:246; and SEQ ID NO:247.

Claim 28 (New): A method of antagonizing an EPO receptor or a method of treating diseases or conditions associated with over-activation of the EPO receptor, comprising administering a composition comprising an EPO variant in amounts sufficient to: 1) block the binding of naturally occurring EPO to its receptor; or 2) reduce the activation levels of the EPO receptor, wherein the EPO variant comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 10, 11, 12, 13, 14, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175,

176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, and 244, and wherein the EPO variant has the ability to bind to the EPO receptor and fails to activate the EPO receptor.

Claim 29 (New): A method of producing a recombinant peptide, polypeptide, protein or antibody comprising the culturing of a host cell according to claim 27 under conditions that allow for the expression of a recombinant peptide, polypeptide, protein or antibody.

Claim 30 (New): The method according to claim 29, further comprising the isolation of the recombinant peptide, polypeptide, protein and/or antibody from the host cell or culture system.

Claim 31 (New): A method for reducing a helper T lymphocyte (HTL) response against a candidate protein comprising: a) selecting a protein; b) analyzing the amino acid sequence of the protein for potential HTL epitopes; and c) modifying the amino acid sequence of the protein by removing the potential HTL epitope and thereby generating an analog protein.

Claim 32 (New): The method according to claim 31, further comprising conducting *in vitro* antigenicity analysis of said candidate protein using helper T-cells.

Claim 33 (New): An isolated, purified, or recombinant polynucleotide comprising a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 10, 11, 12, 13, 14, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210,

211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, and 247.